
Preclinical development of an exhaustion-resistant CAR-T stem cell for cancer immunotherapy

Grant Award Details

Preclinical development of an exhaustion-resistant CAR-T stem cell for cancer immunotherapy

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-13212

Investigator:

Name:	Ansuman Satpathy
Institution:	Stanford University
Type:	PI

Award Value: \$1,420,200

Status: Pre-Active

Grant Application Details

Application Title: Preclinical development of an exhaustion-resistant CAR-T stem cell for cancer immunotherapy

Public Abstract: **Research Objective**

The expected outcome is an exhaustion-resistant CAR-T cell, which persists long-term in a functional progenitor T cell state in the tumor microenvironment and can be used for cancer immunotherapy.

Impact

CAR-T cells are effective in B cell cancer, but less than 50% of patients experience long-term disease control. Exhaustion-resistant CARs may provide long-term benefit that extends to solid tumors.

Major Proposed Activities

- Establish and optimize a CRISPR-engineered CAR-T stem cell therapy that resists T cell exhaustion.
- Perform in vitro evaluation of TEx-resistant CAR-T cell tumor recognition and cytotoxicity, and progenitor cell state characterization, compared to conventional CAR-T cells.
- Perform in vivo evaluation of TEx-resistant CAR-T cell function and persistence in xenograft tumor models, compared to conventional CAR-T cells.
- Perform epigenomic characterization of T cell exhaustion in TEx-resistant CAR-T cell in tumor models, compared to conventional CAR-T cells.

Statement of Benefit to California: A significant barrier to long-term efficacy of cancer immunotherapy is the development of T cell exhaustion, which limits T function in the tumor microenvironment. The proposed exhaustion-resistant CAR-T stem cell therapy candidate has the potential to benefit a large population of patients in California who suffer from a broad range of cancers that may be targeted by CAR-T cells, including solid tumors (lung, prostate, sarcoma, and skin) and blood cancers (leukemia, multiple myeloma, lymphoma).

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